Transadbominal Amnioinfusion In Preterm Prelabor Rupture Of Membrane: A Case Report*

Evita E. Oconer, MD and Joanna Zerline Lozada-Pascual, MD, FPOGS, FPSMFM
Department of Obstetrics and Gynecology, Quirino Memorial Medical Center

ABSTRACT

Premature prelabor rupture of membranes (PPROM) is defined as rupture of membranes before 37 completed weeks. The diagnosis of rupture of membranes can be made by using sterile speculum examination. Amniotic fluid is seen pooling in the posterior fornix or clear fluid is passing from the cervical canal. Presented is a case of PPROM which was managed with transabdominal amniotransfusion. The effects of amnioinfusion on pregnancy outcome in preterm premature rupture of membranes (PPROM) are unclear. Postulated benefits include prolongation of the latency period and prevention of pulmonary hypoplasia and infection. Transabdominal amnioinfusion is a promising procedure. It can be a very useful procedure in special cases, such as, preterm prelabor rupture of membrane to improve neonatal survival and outcome.

INTRODUCTION

Premature prelabor rupture of membranes (PPROM) is defined as rupture of membranes before 37 completed weeks[1]. Patients usually complain of a sudden gush of warm fluid from their vagina or a continuous 'leaking' of water. The diagnosis of rupture of membranes can be made by using sterile speculum examination. Amniotic fluid is seen pooling in the posterior fornix or clear fluid is passing from the cervical canal. Another test that we make use as an indicator is nitrazine. Test papers are impregnated with the dye, and the color of the reaction is interpreted by comparison with a standard color chart. A pH above 6.5 is consistent with ruptured membranes. A ferning test may also be done where in there is visualization of a characteristic 'fern-like' pattern on a slide under the microscope. A small amount of cervical mucus is allowed to air-dry on a clean, glass slide. The cervical mucus forms fern-like patterns due to crystallization of sodium chloride on mucus fibers[2].

It is very important to establish the diagnosis of rupture of membranes for the clinician to adequately formulate a treatment plan. One main concern is the risk of intraamnionic infection which can affect both the mother and the fetus. It has been postulated that antibiotic therapy may significantly decrease the complications associated with infection. But when rupture of membranes occurs before term, several issues need to be considered in coming up with a plan of management. Prematurity is the principal risk to the fetus, while infection morbidity and its complications are the primary maternal risks. Majority of women proceed to active labor and deliver soon after PPROM.

PPROM likely arises from multiple pathologic pathways. Most commonly, chronic inflammation and/or infection increases the production of hormones and cytokines in the uterus, membranes, and/or placenta, which results in preterm contractions, membrane weakening, and PPROM. It has been suggested that repeated stretching of the amniochorion induces a phenomenon that is known as "strain hardening," which makes the membranes less elastic and more susceptible to PPROM. A localized alteration in the amnion and chorion has been identified, and generalized placental and decidual relaxin levels have been shown to be increased in noninfected fetal membranes with PPROM. Relaxin increases local levels of metalloproteinases and tissue plasminogen activator that results in extracellular matrix degradation and rupture. A generalized loss of collagen in the fetal membranes has been associated with a short interval between PPROM and delivery. It was also said that maternal stress has an important effect on the autocrine or paracrine systems that control labor and may play a role in PPROM. [3]

Several areas of controversies exist regarding the best medical approach or management of PPROM. Expectant management and giving of dexamethasone is a prime option. But, there are still other ways to

* Second Place, 2014 Philippine Obstetrical and Gynecological Society (POGS) Interesting Case Contest, May 2, 2014, SMX Convention Center, Lanang, Davao City

potentially manage PPROM that can decrease the risk of neonatal morbidity and eventually lead to a better neonatal outcome. Presented is a case of PPROM which was managed with serial transabdominal amnioinfusion.

CASE REPORT

This is a case of C.G. 42 years old, G6P3 (3023) from Binangonan, Rizal, who came in due to watery vaginal discharge for 6 hours. Few hours prior to consult, patient complained of a sudden gush of watery vaginal discharge. She noted no abdominal pain or uterine contractions. She then went to the lying – in where she was having her prenatal check up, and was advised to transfer to a tertiary hospital due to lack of facilities. Patient then transferred to the nearest tertiary hospital and was advised termination of pregnancy but was informed that they do not have enough facilities to support the baby, hence consulted our institution and was admitted.

Patient had her Prenatal check ups at St. Christian Lying-in three times where she was attended to by an OB-Gyne. At 31 weeks AOG, patient was diagnosed with asymptomatic UTI however no treatment was given. She was regularly taking her Multivitamins, Ferrous sulfate and Calcium supplements.

Past Medical History:

Past medical history is unremarkable

Family Medical History:

Family medical history reveals Diabetes Mellitus type 2 on maternal side and cardiovascular disease on paternal side.

OB-Gyn History:

Patient is a Gravida 6Para 3 (3023), with 3 live births via Cesarean section for cephalo pelvic disproportion and repeat, and 2 for spontaneous abortions where completion curettage was done. Patient had her menarche at age 13, was regularly menstruating using 3-4 pads per day moderately soaked. Her last menstrual period was on September 18, 2012, giving her an amenorrhea of 31 weeks and 5 days.

Personal and Social History:

Patient is currently unemployed and stays at home with her current partner, two children and mother. She is a non smoker and drinks occasionally but not while she was pregnant.

Physical Examination:

BP was 130/70, cardiac rate of 86 respiratory rate of 15, afebrile at 36.9.

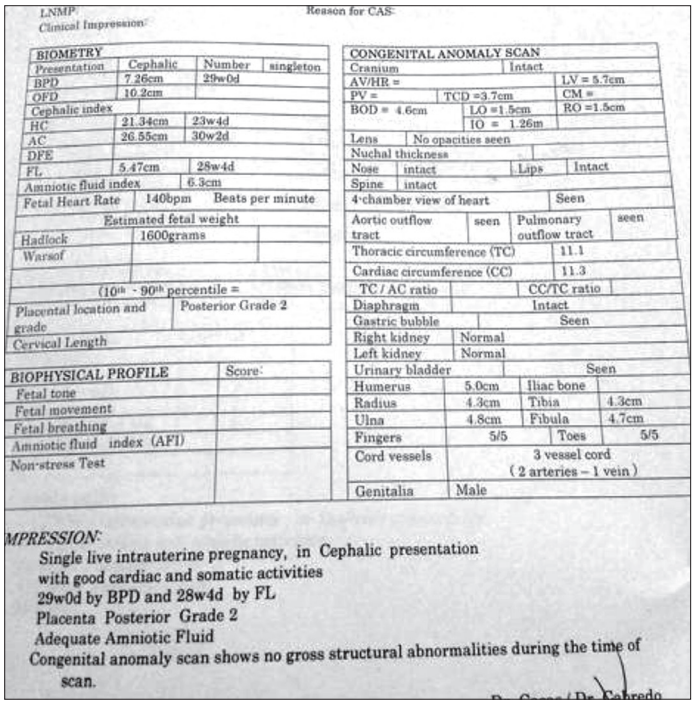
Patient was awake, conscious, coherent, not in cardio respiratory distress. All other organ systems were essentially normal. Abdomen was globular, soft nontender with normoactive bowel sounds. Fundic Height of 25 cm with good fetal heart tones at 140s. on leopold's maneuver, L1 was breech, L2 was fetal back at maternal left / fetal small parts at maternal right L3 was not engaged and L4 was cephalic. On speculum examination cervix was pink, smooth, with no erosions and pooling of clear fluid. On internal examination Cervix was soft and closed.

Primary Impression:

G6P3 Pregnancy Uterine (3023) 31 weeks and 5 days AOG by LMP, cephalic NIL, PPROM x 6 hours; Previous CS unknown type 3x for Cephalopelvic disproportion for CPD and repeat; Poor OB history for 2 spontaneous abortions; Urinary Tract Infection

At the ER, ferning test done was positive. Patient was admitted and transferred to the labor room. She was hooked to IVF D5LR 1L. Diagnostics included a CBC which revealed leukocytosis of 18.3 g/L and Urinalysis with a pyuria of 13-16 / hpf (Table 1). Patient was started on IV antibiotics: Ampicillin 2 gm TIV as loading dose then 1 gm every 6 hours, Gentamycin 240 mg TIV OD and Metronidazole 500 mg TIV every 8 hours . Patient was also given Dexamethasone 6 mg IM every 12 hours for 4 doses. Patient was immediately hooked to the EFM which revealed a reactive NST. Labor watch was done, no contractions noted. A Pediatric notification was also made. An ultrasound was done which revealed a single live intrauterine pregnancy, consistent with 32 weeks age of gestation by fetal biometry with good somatic and cardiac activity with an amniotic fluid index of 2.5 cm. On the 2nd hospital day, transabdominal amnioinfusion was done. BPS was 8/10 pre amnioinfusion for oligohydramnios, NST was reactive (Figure 1). A total of 500 ml of warm PNSS was instilled (Figures 2 & 3). AFI post amnioinfusion was 8.6 cm. A Congenital Anomaly Scan was also done which revealed normal result (Appendix A). Cervical length was 4 cm with no funneling. After which, patient was hooked to

EFM. NST was reactive (Figure 4). BPS was 10/10. For the succeeding hospital days, NST was done every 8 hours which revealed all reactive NST. For high risks patients not in labor, at least a daily NST monitoring is sufficient, however close fetal monitoring was done, because of the fear that anytime this patient would be oligohydramnios again and with a non reactive NST would give a BPS of 6/8 and is an indication to terminate the pregnancy. The 5th hospital day, there was again oligohydramnios, AFI was 2.8 cm, NST reactive, BPS 8/10 (Figure 5). Second amnioinfusion took place. The same procedure was done and a total of 1 liter of warm PNSS was infused (Figures 6 & 7). Post amnioinfusion the AFI was 11.7, and BPS was 10/10, NST reactive (Figure 8). Continous egress of clear amniotic fluid transcervically was still noted. On the 9th hospital day, AFI was 1.7 cm, still with reactive NST (Figure 9). Third amnioinfusion was done with the same procedure however, warm D5LR was used, and a total of 750cc of fluid was instilled (Figures 10 & 11). AFI postamnioinfusion was 8.5 cm. after which, NST was done, revealed reactive (Figure 12) and BPS was 10/10. The third amnioinfusion was the last amnioinfusion. Initially the aim was to carry pregnancy to at least 34 weeks AOG as possible. Subsequent fetal surveillance studies consistently revealed reassuring result with AFI ranging from 5.5 to 8.9 cm (Table 2). There was also adequate fetal growth demonstrated. During transabdominal amnioinfusion, tocolysis was done to prevent uterine contraction from developing secondary to the procedure. Serum electrolytes were also monitors, patient initially was hypokalemic, but



LNMP:
Clinical Impression:
Reason for CAS:

BIOMETRY			
Presentation	Cephalic	Number	singleton
BPD	7.26cm	29w0d	
OFD	10.2cm		
Cephalic index			
HC	21.34cm	23w4d	
AC	26.55cm	30w2d	
DFE			
FL	5.47cm	28w4d	
Amniotic fluid index	6.3cm		
Fetal Heart Rate	140bpm	Beats per minute	
Estimated fetal weight			
Hadlock	1600grams		
Warsof			
(10th - 90th percentile =			
Placental location and grade	Posterior Grade 2		
Cervical Length			

BIOPHYSICAL PROFILE	Score:
Fetal tone	
Fetal movement	
Fetal breathing	
Amniotic fluid index (AFI)	
Non-stress Test	

CONGENITAL ANOMALY SCAN			
Cranium	Intact		
AV/HR =		LV = 5.7cm	
PV =	TCD =3.7cm	CM =	
BOD = 4.6cm	LO =1.5cm	RO =1.5cm	
	IO = 1.26m		
Lens	No opacities seen		
Nuchal thickness			
Nose	intact	Lips	Intact
Spine	intact		
4-chamber view of heart	Seen		
Aortic outflow tract	seen	Pulmonary outflow tract	seen
Thoracic circumference (TC)	11.1		
Cardiac circumference (CC)	11.3		
TC / AC ratio		CC/TC ratio	
Diaphragm	Intact		
Gastric bubble	Seen		
Right kidney	Normal		
Left kidney	Normal		
Urinary bladder	Seen		
Humerus	5.0cm	Iliac bone	
Radius	4.3cm	Tibia	4.3cm
Ulna	4.8cm	Fibula	4.7cm
Fingers	5/5	Toes	5/5
Cord vessels	3 vessel cord (2 arteries – 1 vein)		
Genitalia	Male		

IMPRESSION:
Single live intrauterine pregnancy, in Cephalic presentation with good cardiac and somatic activities
29w0d by BPD and 28w4d by FL
Placenta Posterior Grade 2
Adequate Amniotic Fluid
Congenital anomaly scan shows no gross structural abnormalities during the time of scan.

Appendix A. Congenital Anomaly Scan result

TABLE 1: Diagnostics

Table 1.1 : Hematology

	4/28/13	5/2/13	5/7/13	5/13/13	5/19/13	5/21/13	Normal Values
RBC	4.05	3.64	4.14	4.38	4.10	4.15	4.2-5.4 x 10^12/L
Hemoglobin	123	112	124	138	129	132	120-160 g/L
Hematocrit	0.37	0.34	0.38	0.41	0.38	0.40	0.36-0.47%
MCV	91.6	92.1	92.8	94.1	93.1	95.1	80-96fL
MCH	30.5	30.9	30.0	31.50	31.40	31.70	27-31pg
MCHC	33.2	33.5	32.3	33.5	33.7	33.3	32-36 %
RDW	13.5	14.1	14.1	13.6	13.3	13.5	11.6-14.6
Platelet count	305	320	Adeq	Adeq	Adeq	Adeq	150-45- x10^g/L
WBC	18.13	9.06	10.61	11.4	12.7	13.8	X10^g/L
Neutrophil	0-924	0.681	0.721	0.73	0.74	0.71	0.50-.70
Lymphocytes	0.063	0.233	0.206	0.21	0.19	0.20	0.20-.70
Eosinophil	0.002	0.032	0.025	0.01	0.02	0.02	0.00-.06
Monocyte	0.009	0.053	0.045	0.05	0.05	0.00	0.02-.09
Basophil	0.001	0.001	0.003	0.00	0.00	0.00	0.00-.02

Table 1.2 Urinalysis

	4/28/13	5/21/13	
Color	Yellow	Light yellow	
Transparency	Sl. Turbid	Clear	
Reaction	5.0	5.0	
Specific Gravity	1.030	1.020	
WBC	13-16	6-8	/HPF
RBC	5-8	4-5	/HPF
Epithelial cells	any	Moderate	
Bacteria	Moderate	Moderate	
Mucous threds			
Yeast cells			
Albumin	Negative	Negative	g/L
Sugar	Negative	Negative	Mmol/L
Ketones			Mmol/L
Crystals	Amorphous urates - many		

Table 1.3. Blood Chemistry

	5/4/13	5/7/13
Portassium	2.9	3.7
Glucose	6.7	
Chloride	102	99
Blood urea nitrogen	2.1	
Creatinine	88.4	
Sodium	137	
HBA1C	6.58 %	

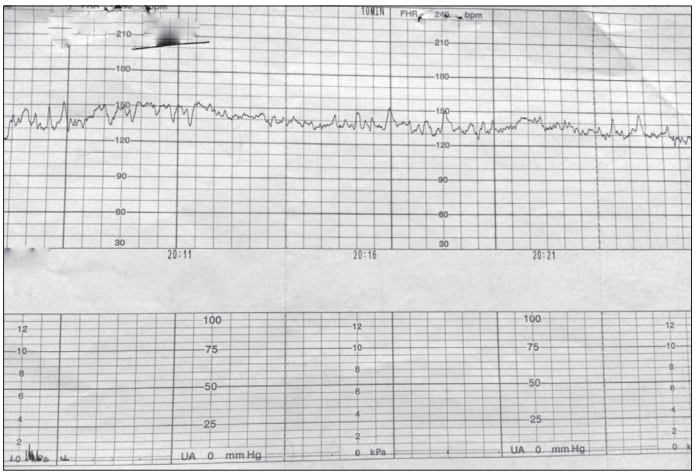


Figure 1. NST 1st Preamnioinfusion

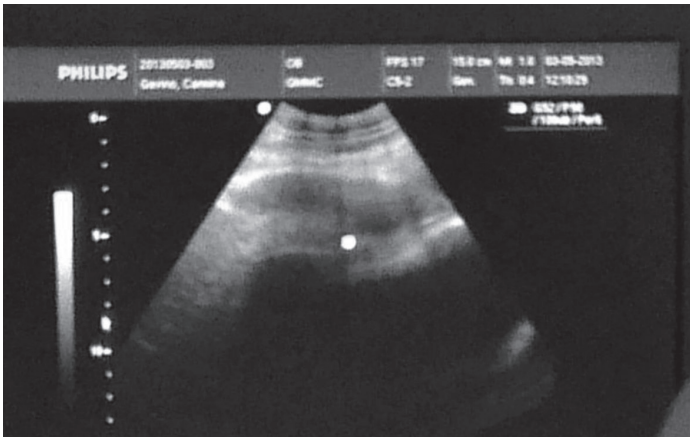


Figure 2. 1st Amnioinfusion

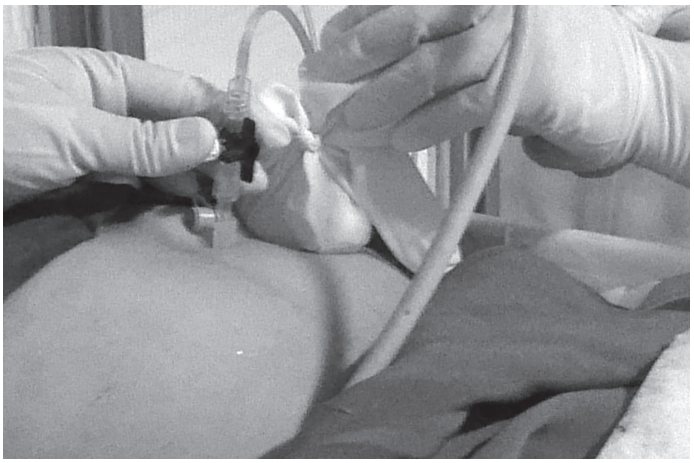


Figure 3. 1st Amnioinfusion

was corrected after three days. In order to monitor if intraamnionic infection is starting to seed in, an ESR and CRP was initially requested, however it was not available in the institution. Complete blood count was requested every 5-7 days instead. And antibiotics were extended up to 14 days. On the 25th hospital day, patient went into preterm labor. Moderate to strong uterine contraction occurring every 4-5 minutes lasting for 60-70 seconds were noted. On internal examination, cervix was dilated to 1 cm,

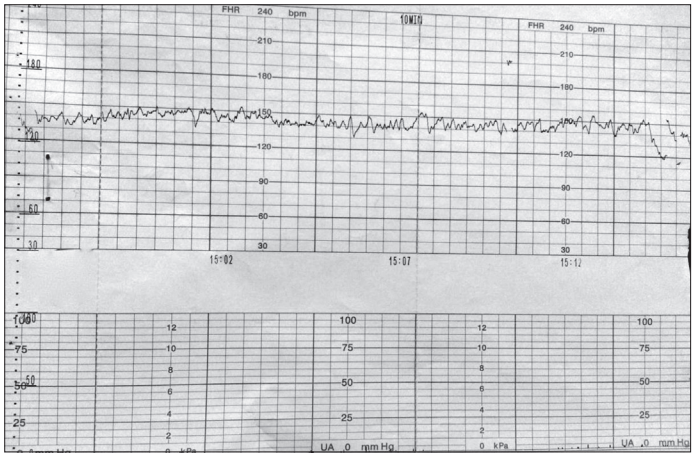


Figure 4. NST 1st Postamnioinfusion

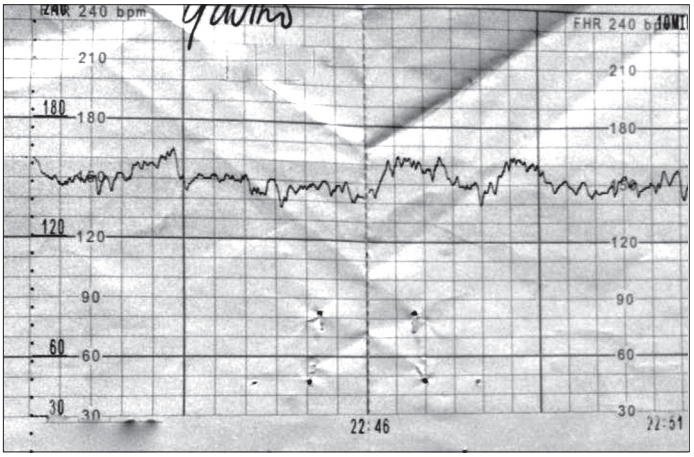


Figure 8. NST 2nd Postamnioinfusion

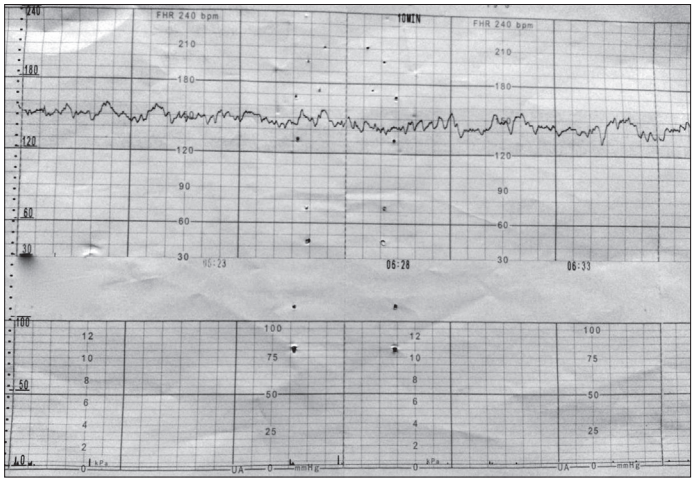


Figure 5. NST 2nd Preamnioinfusion

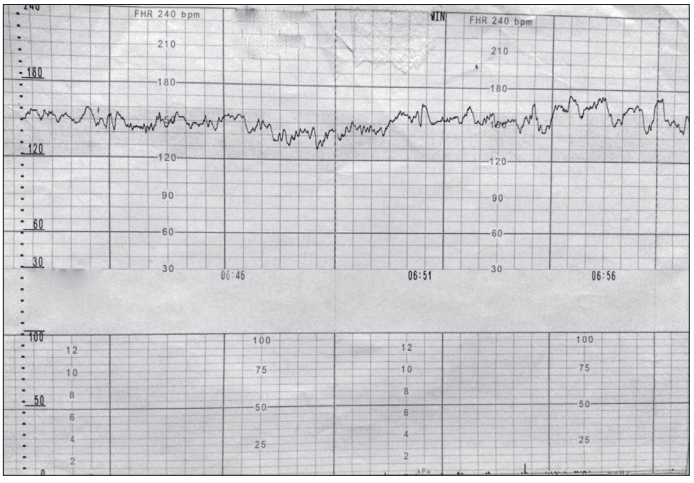


Figure 9. NST 3rd Preamnioinfusion

Figure 6. 2nd Amnioinfusion

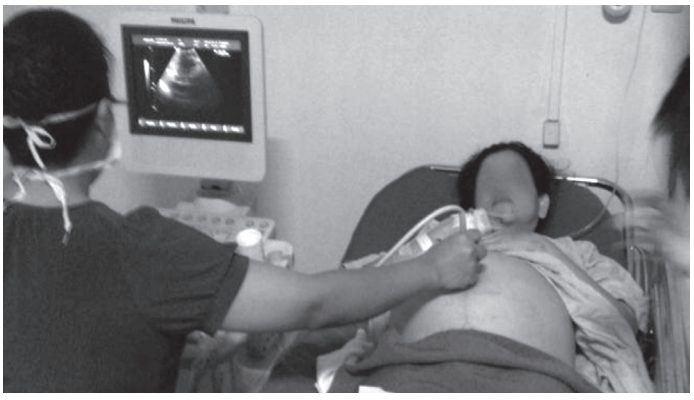


Figure 10. 3rd Amnioinfusion

Figure 7. 2nd Amnioinfusion

Figure 11. 3rd Amnioinfusion

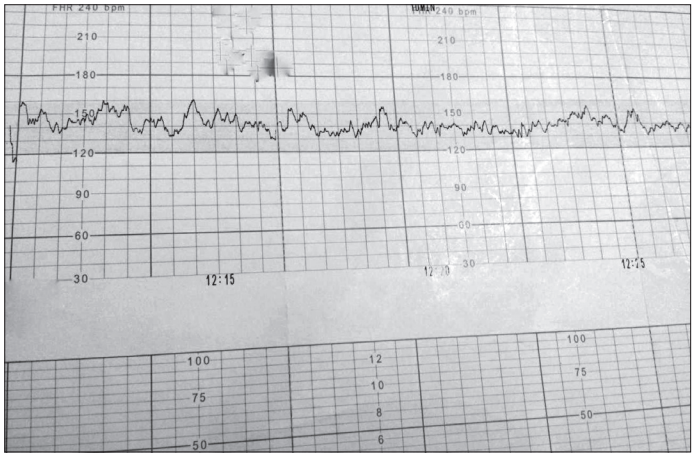


Figure 12. NST 3rd Postamnioinfusion

Figure 13. Baby Boy Apgar Score 9

80% effaced cephalic presentation station -3, with leaking bag of water. Emergency repeat cesarean section was done. The management team included a Perinatologist, Anesthesiologist and a Neonatologist. Patient delivered to a live baby boy, Apgar Score 9, Birth weight of 1.95 kgs and a pediatric aging of 36 weeks (Figure 13).

DISCUSSION

Amnioinfusion is infusion of normal saline to increase intraamnionic fluid. It can be a prophylactic, diagnostic, or therapeutic intervention. Potential indications includes [4] : (a) Prevention and treatment of repetitive variable decelerations (b) prevention of meconium aspiration (c) improved visualization during sonographic or fetoscopic assessment of fetal anomalies (d) treatment for oligohydramnios or prevention of chorioamnionitis in premature rupture of membranes.

Transcervical amnioinfusion is a more common route of amnioinfusion. It is done when a woman is in labor and a transcervical catheter is inserted vaginally. While on the other hand, transabdominal amnioinfusion is usually done in a non parturient patient. However an anteriorly implanted placenta is contraindicated and an ultrasound guided approach is highly recommended. Studies have shown that there are no significant difference in neonatal outcome between transcervical and transabdominal approach.

Transabdominal amnioinfusion is usually done when a patient is not in labor. Using a large bore catheter, it is inserted abdominal with an ultrasound to guide the whether the amniotic sac has been already reached. Then a venoset is connected to the needle and the fluid is instilled. Complications include going into preterm labor, abruptio placenta, infection and injury to the fetus.

Table 2. Amniotic Fluid Index Monitoring

Hospital Days	Amniotic Fluid Index
1	2.5 cm
2	1.02 cm to 8.6 cm
3	5.7 cm
4	2.8 cm
5	2.8 cm to 11.6 cm
6	4.2 cm
7	2.4 cm
8	1.7 cm
9	1.7 cm to 8.5 cm
10	8 cm
11	9 cm
12	6.3 cm
13	5.5 cm
14	5.6 cm
15	5.5 m
16	5.9 cm
17	6.2 cm
18	8.3 cm
19	7.8 cm
20	8.9 cm
21	8 cm
22	7.9 cm
23	8.1 cm
24	5 cm

Oligohydramnios is defined as an amniotic fluid index of < 5 cm. AFI was determined using the sum total of the deepest vertical pockets in each of the four quadrants into which the uterus is divided by using the umbilicus and the linea nigra as reference points for the upper and lower halves and for the left and right halves, respectively. The ultrasound transducer is placed perpendicularly to the patient's table and in a sagittal plane to the patient herself. Each amniotic pocket was free of fetal extremities and umbilical cord. [5]

Oligohydramnios is most often associated with obstruction of the fetal urinary tract and renal agenesis. It is believed that in the first trimester of pregnancy, amniotic fluid is from the transudate of plasma, either from the fetus through the non keratinized fetal skin, or from the mother across the uterine decidua or placenta surface, or both. In the latter part of pregnancy, the major contributors of amniotic fluid is the fetal urine. The second major source of amniotic fluid is fetal lung fluid. Under physiologic conditions, half of the fluid secreted by the lungs becomes part of the amniotic fluid. But, normal lung expansion is only possible if the alveolus is also filled with enough fluid. In a condition called pulmonary hypoplasia, the number of airways are decreased. The normal fetal lung fluid volume is not maintained, and the fetal lung fail to have a normal frequency and amplitude of fetal breathing movement for it to grow normally. Oligohydramnios can cause a decrease in fetal lung fluid by external chest compression. Oligohygdramnios occurring at an earlier age of gestation, specifically at 16-24 weeks AOG (Canalicular stage) the more severe the pulmonary hypoplasia is. [3]

The effects of amnioinfusion on pregnancy outcome in preterm premature rupture of membranes (PPROM) are unclear. Postulated benefits include prolongation of the latency period and prevention of pulmonary hypoplasia and infection. A study by Tranquilili at al., which included 34 women reported treatment with transabdominal amnioinfusion after PPROM resulted in significant prolongation of pregnancy and better neonatal outcomes compared to standard expectant management. [6]

Another study by De Carolis et al., they determined the effects of amnioinfusion treatment on fetal and neonatal mortality and neonatal pulmonary development in women with singleton pregnancies and premature rupture of the membranes occurring at a gestational age of <26 weeks and who had severe oligohydramnios. Results show that there was a higher number of live births in the treated group, especially with a gestational age of rupture of <20 weeks. Furthermore, even if GAR (Gestational Age of Rupture) is an important factor for predicting pulmonary hypoplasia, amnioinfusion treatment reduced the probability of pulmonary hypoplasia. In fact, for gestations over 20 weeks, amnioinfusion treatment significantly reduced the risk of pulmonary hypoplasia even if normal lung development cannot be guaranteed. [7]

The idea of transabdominal amnioinfusion in this case was promising. Patient was not in labor, had oligohydramnios due to premature prelabor rupture of membranes, NST were all reactive, and the placenta was implanted posteriorly with no previa. The first amnioinfusion successfully raised the amniotic fluid index from 2.5 to 8.6 cm. However, with continuous spontaneous egress of fluid transcervically, AFI decreased again to 2.8 cm after just two days. Thus, serial amnioinfusion was considered. Several studies have been published regarding the benefits of serial amnioinfusion. In a study by Tan et al., it was seen that serial amnioinfusion allowed prolongation of pregnancy in about 75%, with an attendant decrease in the risk of pulmonary hypoplasia. [8]

In another study by Vergani et al., on the role of amnioinfusion in the management of oligohydramnios in PPROM <26 weeks AOG, it was shown that patients in the persistent oligohydramnios group had a significantly shorter interval to delivery, lower neonatal survival (20%), and higher rates of pulmonary hypoplasia (62%) and abnormal neurologic outcomes (60%) than the patients in the groups in which amnioinfusion was not necessary or was successful. They concluded that, pregnancies with preterm premature rupture of membranes related oligohydramnios at <26 weeks gestation in which serial amnioinfusions successfully alleviate oligohydramnios have a perinatal outcome that is significantly better than the outcome in those with persistent oligohydramnios and is comparable with gestations with preterm premature rupture of membranes in which oligohydramnios never develops. In the persistent oligohydramnios group, successful procedures and prenatal administration of corticosteroids are the only independent predictors

of perinatal survival. [9]

On the third amnioinfusion, a different fluid was used. There have been several debates regarding the fluid to be used in amnioinfusion, but studies have shown that there is no significant difference between the use of plain saline solution over 5% dextrose lactated ringer. In a study by Pressman et al., they compared the effects of intrapartum amnioinfusion with normal saline solution versus lactated Ringer's solution plus physiologic glucose on neonatal electrolytes and acid-base balance. They concluded that intrapartum amnioinfusion with normal saline solution or lactated Ringer's solution plus physiologic glucose has no effect on neonatal electrolytes or acid-base balance. [10]

What brought about the ability to sustain the fluid during the third amnioinfusion? There are two things to contemplate upon: 1) Is it because of the change of fluid used as a medium for the procedure or 2) Has the membrane spontaneously sealed off. As mentioned earlier the use of D5LR versus Plain NSS has no significant difference. However we should take into account the difference of their composition. With the D5LR, a sugar containing fluid, it could be that the fluid moved more slowly due to osmolality. But even though this is the case, it would be that it would only take a few more days compared to PNSS for the leaking to occur. Second, the fetal membrane had spontaneously sealed off. The fetal membrane form an adjustable bio-container that provides the fetus with a limited space that is filled with amniotic fluid that allows movement. They also protect the growing fetus against infection, trauma, and toxins. The strength of the tissue is provided predominantly by the collagen in the amnion, although the amnion and chorion together are stronger than either layer alone. Because the fetal membranes are not innervated and only very poorly vascularized, a typical wound healing response that includes inflammation, scar formation, and tissue regeneration which what happens in skin healing and many other organs is unlikely to occur.

Some patients with spontaneous PPROM cease to leak amniotic fluid. These patients also have good pregnancy outcomes as they are delivered at a mean gestational age of 38 weeks. In the study of Devilieger et al., which stated that fetal membranes have the capacity to seal a created or spontaneously occurring defect. However, the leakage could be concealed, or the membranes could reseal through retraction, sliding, contraction, and scarring in the myometrial and decidual layers of the uterus, rather than involving an active healing mechanism at the level of the fetal membranes. They found out that cell monolayers that are obtained from an amnion-derived cell line were found to be capable of repairing a central microsurgical defect, with 75% to 80% of the defect being repaired within 24 hours. In amniocytes that are obtained from digested fresh human fetal membranes, the repair capacity of these monolayers was found to be gestational age dependent, with cells that are obtained at earlier gestational ages showing higher proliferation rates and faster closure of the central defect.

Fetal membrane repair is a very difficult aspect to study in the field of obstetrics, so despite the magnitude of this problem only a few centers have taken up the challenge to find out if indeed spontaneous healing of the membrane thus happens. However in some literature, they state that it happens less than 10% of the time.

CONCLUSION AND RECOMMENDATION

Serial Transabdominal Amnioinfusion, though an invasive procedure, is a very promising way of increasing neonatal survival. The ultimate goal to bring the pregnancy to as close to term is possible was achieved. Even though it was recommended to terminate the pregnancy at 34 weeks, it was taken into consideration the condition which the baby will be living into.

In the course of the case, two hypothesis was made. First, with regard to the fetal membrane, it is unlikely that the membrane had sealed off or had completely healed. However, as the previous literature have stated, the membrane has the capacity to retract if not to heal completely. Retraction of the membrane would not prevent egress of amniotic fluid, but it may slow down the process. As said, fetal membrane study is a very difficult aspect to explore, but with advancing technologies and with the continuing efforts of maternal-fetal medical researchers, it is a bright future. Second, even though studies have shown that the use of D5LR compared to PNSS has no significant difference, it can not be disregarded that due to the sugar component of D5LR, its movement was slower due to its higher osmolality and fetal ingestion of the fluid contributed

to fetal growth and ultimately, allowing the fetus to produce urine.

In the future, if given again a chance to do the procedure, D5LR will be the first choice of fluid to use. An ESR and CRP would have been a very useful tool to help monitor if an infection is starting to set in.

Transabdominal amnioinfusion is a promising procedure. It can be a very useful procedure in special cases, such as this, with preterm prelabor rupture of membranes to improve neonatal survival and outcome. Is it being heroic? For us, optimistic is more appropriate.

REFERENCES

1. Cunningham et al., *Williams Obstetrics* 23rd edition, Texas, USA, 2010

2. R. Devlieger,MD eta al. "Fetal membrane healing after spontaneous and iatrogenic membrane rupture: A review of current evidence". http://www.ncbi.nlm.nih.gov

3. D. Gramellini eta al.,2004. "Ultrasound evaluation of amniotic fluid volume: methods and clinical accuracy". *Acta Bio Medica Ateneo Parmanese* 2004; 75; Suppl. 1: 40-44

4. Creasya and Resnik's *Maternal-Fetal Medicine Principles and Practice*, 6th edition, 2009.

5. Tranquilili et al, 2005. "Transabdominal amnioinfusion in preterm premature rupture of membrane: a randomized control trial.:" *BJOG* 2005 Jun; 112(6).

6. De Carolis et al., 2006. "Is there significant improvement in neonatal outcome after treating PPROM mothers with amnioinfusion?. *Biological neonate* 2004

7. Tan et al., 2003. "Test Amnioinfusion to Determine Suitability for Serial Therapeutic Amnioinfusion in Midtrimester Premature Rupture of Membranes". *Fetal Diagnostic Therapy* 2003.

8. Vergani et al., 2004. "Premature rupture of the membranes at < 26 weeks: role of amnioinfusion in the management of oligihydramnios" Department of Obstetrics and Gynecology, San Gerardo Hospital, Monza, Italy.

9. Pressman et al., 1996. "A Prospective Randomized Trial Of Two Solutions For Intrapartum Amnioinfusion: Effects On Fetal Electrolytes, Osmolality, And Acid-Base Status." *American Journal of Obstetrics and Gynecology* October 1996.

10. R. Devlieger,MD eta al."Fetal membrane healing after spontaneous and iatrogenic membrane rupture: A review of current evidence". http://www.ncbi.nlm.nih.gov